



Exon 1

... 9408 nt ...

Exon 3 Coordinates: 527d12\_Contig308G 21141-20945

... 6094 nt ...

... 1827 nt ...

Exon 5 Coordinates: 527d12\_Contig308G 13220-13088 tttctcagTCCACACTCGCTGTGAGGAGGACAATGGCGGCTGCTCCCACCTGTGCCTGCTGCCCAAGCGAGCCTTTCTACACATGCGCCTGCCCCACGGTGTGCAGCTGCAGGACAACGGCAGGACGTGTAAGGCAGgtgaggcggtgggacg



... 20923 nt ...

Exon 6 Coordinates: 527d12\_Contig309G 7705-8100

ctccacagGAGCCGAGGAGGTGCTGCTGCTGCCCGGCGGACGGACCTAC
GGAGGATCTCGCTGGACACGCCGGACTTCACCGACATCGTGCTGCAGG
TGGACGACATCCGGCACGCCATTGCCATCGACTACGACCCGCTAGAGG
GCTATGTCTACTGGACAGATGACGAGGTGCGGGCCATCCGCAGGGCG
TACCTGGACGGTCTGGGGCGCAGACGCTGGTCAACACCGAGATCAA
CGACCCCGATGGCATCGCGGTCGACTGGCCCGAAACCTCTACTG
GACCGACACGGGCACGGACCGCATCGAGGTGACGCCCTCAACGGCA
CCTCCCGCAAGATCCTGGTGTCGGAGGACCTTGGACGACCCCGAGCC
ATCGCACTGCACCCCGTGATGGGgtaagacgggc

..... 3211 nt .....

Exon 7 Coordinates: 527d12\_Contig309G 11311-11482
ttcttctccagCCTCATGTACTGGACAGACTGGGGAGAGAACCCTAAAATCGA
GTGTGCCAACTTGGATGGGCAGGAGCGGCGTGTGCTGGTCAATGCCTC

CCTCGGGTGGCCCAACGCCTGGCCCTGGACCTGCAGGAGGGGAAGC TCTACTGGGGAGACCCAAGACAGACAGATCGAGgtgaggctcctgtgg

..... 13445 nt .....

Exon 8 Coordinates: 527d12\_Contig309G 24927-25143

cegteetgeagGTGATCAATGTTGATGGGACGAAGAGGCGGACCCTCCTGGA GGACAAGCTCCCGCACATTTTCGGGTTCACGCTGCTGGGGGACTTCAT CTACTGGACTGACTGGCAGCGCCGCAGCATCGAGCGGGTGCACAAGG TCAAGGCCAGCCGGGACGTCATCATTGACCAGCTGCCCGACCTGATGG GGCTCAAAGCTGTGAATGTGGCCAAGGTCGTCGgtgagtccggggggtc

....2826 nt .....

Exon 9 Coordinates: 527d12 Contig309G 27969-28256

gttegetteeagGAACCAACCCGTGTGCGGACAGGAACGGGGGGTGCAGCCA CCTGTGCTTCTCACACCCCACGCAACCCGGTGTGGCTGCCCCATCGG CCTGGAGCTGCTGAGTGACATGAAGACCTGCATCGTGCCTGAGGCCTT CTTGGTCTTCACCAGCAGAGCCGCCATCCACAGGATCTCCCTCGAGAC CAATAACAACGACGTGGCCATCCCGCTCACGGGCGTCAAGGAGGCCTC AGCCCTGGACTTTGATGTGTCCAACAACCACATCTACTGGACAGACGT CAGCCTGAAGgtagcgtgggc

.....3102.....

FIG. 3B



Exon 10 Coordinates: 527d12\_Contig309G 31358-31582
cctgetgecagACCATCAGCCGCGCCTTCATGAACGGGAGCTCGGTGGAGCA
CGTGGTGGAGTTTGGCCTTGACTACCCCGAGGGCATGGCCGTTGACTG
GATGGGCAAGAACCTCTACTGGGCCGACACTGGGACCAACAGAATCGA
AGTGGCGCGGCTGGACGGCAGTTCCGGCAAGTCCTCGTGTGGAGGG
ACTTGGACAACCCGAGGTCGCCTGGCCCTGGATCCCACCAAGGGgtaagtgtt
tgectgtc

.....1297 nt.....

Exon 11 Coordinates: 527d12\_Contig309G 32879-33064

.....2069 nt.....

Exon 12 Coordinates: 527d12\_Contig309G 35133-35454

gtgttcatgcagGTCAGGAGCGGGTCGTGATTGCCGACGATCTCCCGCACCCG
TTCGGTCTGACGCAGTACAGCGATTATATCTACTGGACAGACTGGAAT
CTGCACAGCATTGAGCGGGCCGACAAGACTAGCGGCCGGAACCGCAC
CCTCATCCAGGGCCACCTGGACTTCGTGATGGACATCCTGGTGTTCCA
CTCCTCCCGCCAGGATGGCCTCAATGACTGTATGCACAACAACGGGCA
GTGTGGGCAGCTGTGCCTTGCCATCCCGGCGGCCACCGCTGCGGCT
GCGCCTCACACTACACCCTGGACCCCAGCAGCCGCAACTGCAGCCgtaag
tgcctcatggt

......2006 nt.....

Exon 13 Coordinates: 527d12 Contig309G 37460-37659

gcetcetctaCGCCCACCACCTTCTTGCTGTTCAGCCAGAAATCTGCCATCAG TCGGATGATCCCGGACGACCAGCACAGCCCGGATCTCATCCTGCCCCT GCATGGACTGAGGAACGTCAAAGCCATCGACTATGACCCACTGGACAA GTTCATCTACTGGGTGGATGGGCGCCAGAACATCAAGCGAGCCAAGGA CGACGGGACCCAGgcaggtgccctgtgg

.....6965 nt.....

FIG. 3C



Exon 14 Coordinates: 527d12\_Contig309G 44624-44832 ctttgtcttacagCCCTTTGTTTTGACCTCTCTGAGCCAAGGCCAAAACCCAGAC AGGCAGCCCACGACCTCAGCATCGACATCTACAGCCGGACACTGTTC TGGACGTGCGAGGCCACCAATACCATCAACGTCCACAGGCTGAGCGG GGAAGCCATGGGGGTGCTGCGTGCGTGGGGACCGCGACAAGCCCAGGG CCATCGTCGTCAACGCGGAGCGAGGGTaggaggccaac

.....1404 nt.....

Exon 15 Coordinates: 527d12\_Contig309G 46236-46427
ccaccetccegeagGTACCTGTACTTCACCAACATGCAGGACCGGGCAGCCAA
GATCGAACGCGCAGCCCTGGACGGCACCGAGCGCGAGGTCCTCTTCA
CCACCGGCCTCATCCGCCCTGTGGCCCTGGTGGTGGACAACACACTGG
GCAAGCTGTTCTGGGTGGACGCGGACCTGAAGCGCATTGAGAGCTGT
GACCTGTCAGgtacgcgccccgg

.....686 nt.....

Exon 16 Coordinates: 527d12\_Contig309G 47113-47322
ggctgcttgcagGGCCAACCGCCTGACCCTGGAGGACGCCAACATCGTGCA
GCCTCTGGGCCTGACCATCCTTGGCAAGCATCTCTACTGGATCGACCG
CCAGCAGCAGCAGTGATCGAGCGTGTGGAGAAGACCACCGGGGACAAGC
GGACTCGCATCCAGGGCCGTGTCGCCCACCTCACTGGCATCCATGCAG
TGGAGGAAGTCAGCCTGGAGGAGTTCTgtacgtgggggg

.....3884 nt......

Exon 17 Coordinates: 527d12\_Contig309G 51206-51331 ttgtctttgcagCAGCCCACCCATGTGCCCGTGACAATGGTGGCTGCTCCCACA TCTGTATTGCCAAGGGTGATGGGACACCACGGTGCTCATGCCCAGTCC ACCTCGTGCTCCTGCAGAACCTGCTGACCTGTGGAGgtaggtgtgacctaggtgc

....3905 nt.....

.....3052 nt.....

FIG. 3D



Exon 19 Coordinates: 527d12 Contig309G 58524-58634  $tete ett geag {\color{blue} CCATCTGCCCAACCAGTTCCGGTGTGCGAGCGGCCAGT} \\$ GTGTCCTCATCAAACAGCAGTGCGACTCCTTCCCCGACTGTATCGACG **GCTCCGACGAGCTCATGTGTGgtgagccagctt** .....1448 nt..... Exon 20 Coordinates: 527d12 Contig309G 60082-60319  $gtttgtctctggcag {\color{blue}AAATCACCAAGCCGCCCTCAGACGACGACCACCACA} \\$ GGGTGGTGTCTATTTTGTGTGCCAGCGCGTGGTGTGCCAGCGCTATGC GGGGGCCAACGGGCCCTTCCCGCACGAGTATGTCAGCGGGACCCCGC ACGTGCCCCTCAATTTCATAGCCCCGGGCGGTTCCCAGCATGGCCCCT **TCACAG**gtaaggagcctgagatatggaa ....1095 nt..... Exon 21 Coordinates: 527d12\_Contig309G 61414-61552 cttccctgccagGCATCGCATGCGGAAAGTCCATGATGAGCTCCGTGAGCCTG ATGGGGGCCGGGGCGGGTGCCCCTCTACGACCGGAACCACGTCAC AGGGGCCTCGTCCAGCAGCACGAAGGCCACGCTGTACCC GCCGgtgagggggggg .....6513 nt..... Exon 22 Coordinates: 527d12 Contig309G 68065-68162 ttggctctcctcagATCCTGAACCCGCCCCCCCCCGGCCACGGACCCCTCCC TGTACAACATGGACATGTTCTACTCTTCAAACATTCCGGCCACTGCGA **GACCGTACAG**gtaggacatccctgcag .....2273 nt.....

FIG. 3E



Exon 23 Coordinates: 527d12 Contig309G 70435-70901

FIG. 3F



# Model for a LDL Receptor-Related protein, Zmax1

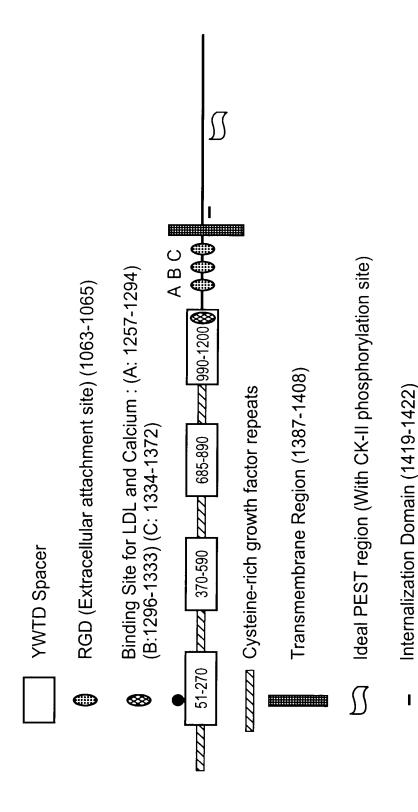


FIG. 4

Site of Glycine to Valine change in HBM allele

I



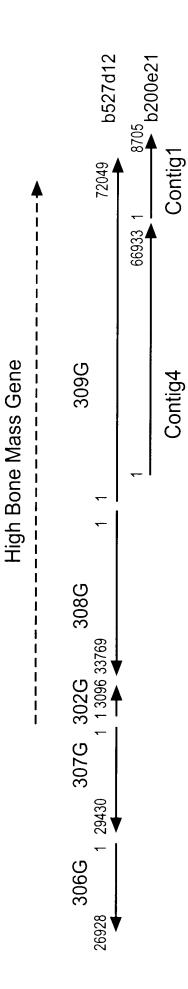


FIG. 5



## FIG. 6A

61	ACTAAAGCGCCGCCGCCGCCATGGAGCCCGAGTGAGCGCGGGCGCGGGCCCGTCCGGCC GCCGGACAACATGGAGGCAGCGCCGCCCGGGCCGCCGCTGCTGCTGCTGCTGCTGCTGC	60 120 17
121 18	GCTGCTGCTGCGGCTGCCCGGCCCCCGCGGCCTCGCCGCTCCTGCTATT	180
181 38	TGCCAACCGCCGGGACGTTGGTGGACGCCGGCGGAGTCAAGCTGGAGTCCACCAT A N R R D V R L V D A G G V K L E S T I	240 57
241 58	CGTGGTCAGCGGCCTGGGCCGCAGTGGACTTCCAGTTTTCCAAGGGAGCCGT V V S G L E D A A A V D F Q F S K G A V	300
301	GTACTGGACAGAGGCGAGGCCATCAAGCAGACCTACCTGAACCAGACGGGGGC Y W T D V S E E A I K Q T Y L N Q T G A	360
361 98	CGCCGTGCAGAACGTGGTCTCTCCCGACGGCCTCGCCTGCGACTG A V Q N V I S G L V S P D G L A C D W	420
421 118	GGTGGGCAAGAAGCTGTACTGGACGCGATCAGAGCCCAACCT V G K K L Y W T D S E T N R I E V A N L	480 137
481 138	CAATGGCACATCCCGGAAGGTGCTCTTCTGGCAGGACCTTGACCAGCCGAGGGCCATCGC N G T S R K V L F W Q D L D Q P R A I A	540 157
541 158	CTTGGACCCCGCTCACGGGTACATGTACTGGACAGACTGGG $oldsymbol{G}$ TGAGACGCCCCGGATTGALL $oldsymbol{L}$ $oldsymbol{D}$ $oldsymbol{P}$ $oldsymbol{A}$ $oldsymbol{M}$ $oldsymbol{Y}$ $oldsymbol{W}$ $oldsymbol{V}$ $oldsymbol{W}$ $oldsymbol{G}$	600

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## FIG. 6B

601	GCGGGCAGGGATGGCAGCACCCGGAAGATCATTGTGGACTCGGACATTTACTGGCC R A G M D G S T R K I I V D S D I Y W P	660 197
661	CAATGGACTGACCTGGAGGAGCAGAAGCTCTACTGGGCTGACGCCAAGCTCAG $_{ m N}$ $_{ m N}$ $_{ m C}$ $_{ m L}$ $_{ m I}$ $_{ m L}$ $_{ m S}$ $_{ m L}$	720
721 218	CTTCATCCACCGTGCCAGACGGCTCGTTCCGGCAGAAGGTGGTGGAGGCAGCCT FIHRANLDGSFRQKVVEGSL	780
781 238	GACGCACCCCTTCGCCCTCTCCGGGGACACTCTGTACTGGACAGACTGGCAGAC T H P F A L T L S G D T L Y W T D W Q T	840 257
841 258	CCGCTCCATCCATGCCTGCAACAAGCGCGCGGGGGGGAAGGAGGAGATCCTGAGTGC R S I H A C N K R T G G K R K E I L S A	900
901	CCTCTACTCACCCATGGACATCCAGGTGCTGAGCCAGGCGGCAGCCTTTCTTCCACAC	960 297
961 298	TCGCTGTGAGGAGACAATGGCGGCTGCTCCCCACCTGCTGCTGCTCCCCAAGCGAGCCRAGCGAGCCCACCTGCTGCTGCTGCTCCCCAAGCGAGCCACCTGCTGCTGCTGCTGCTCCCCAAGCGAGCC	102
1021 318	TTTCTACACATGCGCCCCACGGGTGTGCAGCTGCAGGACAGGGACGTGTAA F Y T C A C P T G V Q L Q D N G R T C K	108( 337
1081	GGCAGGAGCCGAGGAGGTGCTGCTGCCCGGCGGACGGACCTACGGAGGATCTCGCT A G A E E V L L L A R R T D L R R I S L	114(



## FIG. 6C

1141 358	GGACACGCCGGACTTCACCGACATCGTGCTGCAGGTGGACGACGCCGCCACTTGC D T P D F T D I V L Q V D D I R H A I A	1200 377
1201 378	CATCGACTACGACCCGCTAGGGCTATGTCTACTGGACAGATGACGAGGTGCGGGCCATID DYD PLEGYVYWTDDEVEN	1260 397
1261 398	CCGCAGGGCGTACCTGGGGTCTGGGCGCAGACGCTGGTCAACACCGAGATCAACGA R R A Y L D G S G A Q T L V N T E I N D	1320
1321 418	CCCCGATGGCATCGCGTGGGTGGCCCGAAACCTCTACTGGACCGACACGGGCAC	1380
1381 438	GGACCGCATCGAGGTGACGCCTCAACGCCACCTCCCGCAAGATCCTGGTGTCGGAGGA D R I E V T R L N G T S R K I L V S E D	1440 457
1441 458	CCTGGACGAGCCCATCGCACTGCACCCCGTGATGGGCCTCATGTACTGGACAGA	1500
1501 478	CTGGGGAGAGACCCTAAAATCGAGTGTGCCAACTTGGATGGGCAGGGGGGGG	1560 497
1561 498	GGTCAATGCCTCCCTCGGCTGGCCCCAACGGCCCTGGCAGGGGGGGAAGCT V N A S L G W P N G L A L D L Q E G K L	1620 517
1621 518	CTACTGGGGAGACGACAGACAAGATCGAGGTGATCAATGTTGATGGGACGAAGAG Y W G D A K T D K I E V I N V D G T K R	1680 537

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## FIG. 6D

1681 538	GCGGACCCTCCTGGAGGACAAGCTCCCGCACATTTTCGGGGTTCACGCTGCTGGGGGACTT R I L L E D K L P H I F G F T L L G D F	1740
1741 558	CATCTACTGGACTGGCAGCGCCGCAGCAGGGTGCACAAGGTCAAGGCCAGG I Y W T D W Q R R S I E R V H K V K A S	1800
1801 578	CCGGGACGTCATTGACCAGCTGCCCGACCTGATGGGGCTCAAAGCTGTGAATGTGGC R D V I I D Q L P D L M G L K A V N V A	1860 597
1861 598	CAAGGTCGTCGGAACCCGTGTGCGGACAGGAACGGGGGGGG	1920 617
1921 618	CTTCACACCCCACGCAACCCGGTGTGGCTGCCCCATCGGCCTGGAGCTGCTGAGTGACAT F T P H A T R C G C P I G L E L L S D M	1980
1981 638	GAAGACCTGCATGCCTGAGGCCTTCTTGGTCTTCACCAGCAGCCGCCATCCACAG K T C I V P E A F L V F T S R A A I H R	2040
2041 658	GATCTCCCTCGAGACCAACGACGTGGCCATCCCGCTCACGGGCGTCAAGGAGGC I S L E T N N D V A I P L T G V K E A	2100
2101 678	CTCAGCCCTGGACTTTGATGTGTCCAACCACATCTACTGGACAGACGTCAGCCTGAA S A L D F D V S N N H I Y W T D V S L K	2160
2161 698	GACCATCAGCCGCCTTCATGAACGGGAGCTCGGTGGAGCACGTGGTGGAGTTTGGCCT ${ m T}$ ${ m I}$ ${ m S}$ ${ m R}$ ${ m A}$ ${ m F}$ ${ m M}$ ${ m N}$ ${ m G}$ ${ m S}$ ${ m S}$ ${ m V}$ ${ m E}$ ${ m H}$ ${ m V}$ ${ m V}$ ${ m E}$ ${ m F}$ ${ m G}$ ${ m L}$	2220

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## FIG. 6E

2221 718	TGACTACCCCGAGGGCATGGCCGTTGACTGGGCAAGAACCTCTACTGGGCCGACAC D Y P E G M A V D W M G K N L Y W A D T	2280 737
2281 738	TGGGACCAACAGAAGTGGCGGCGGCTGGACGGGCAGTTCCGGCAAGTCCTCGTGTG G T N R I E V A R L D G Q F R Q V L V W	2340
2341 758	GAGGGACTTGGACACCCGAGGTCGCTGGCCTGGATCCCACCAAGGGCTACATCTACTG R D L D N P R S L A L D P T K G Y I Y W	2400
2401 778	GACCGAGTGGGCGGCCAAGCCGAGGATCGTGGGGCCTTCATGGACGGGACCAACTGCAT T E W G G K P R I V R A F M D G T N C M	2460
2461 798	GACGCTGGTGGACAGGGCCGGGCCAACGACCTCACCATTGACTACGCTGACCAGCG T L V D K V G R A N D L T I D Y A D Q R	2520
2521 818	CCTCTACTGGACCTGGACACCAACATGATCGAGTCGTCCAACATGCTGGGTCAGGA L Y W T D L D T N M I E S S N M L G Q E	2580 837
2581 838	GCGGGTCGTGATTGCCGACGATCTCCGCACTCCGGTCTGACGCAGTACAGCGATTA R V V I A D D L P H P F G L T Q Y S D Y	2640 857
2641 858	TATCTACTGGACAGAATCTGCACAGCATTGAGCGGGCCGACAAGACTAGCGGCCG	2700
2701 878	GAACCGCACCTCATCCAGGGCCACCTGGACTTCGTGATGGACATCCTGGTGTTCCACTC	2760

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#### FIG. 6F

2761 898	CTCCCGCCAGGATGGCCTCAATGACTGTATGCACAACAACAGGGCAGTGTGGGCAGCTGTG S R Q D G L N D C M H N N G Q C G Q L C	2820 917
2821 918	CCTTGCCATCCCCGGCGGCTGCGGCTGCGCCTCACACTACACCCTGGACCCCAG L A I P G G H R C G C A S H Y T L D P S	2880 937
2881 938	CAGCCGCAACTGCAGCCCGCCCACCTTCTTGCTGTTCAGCCAGAAATCTGCCATCAG S R N C S P P T T F L L F S Q K S A I S	2940 957
2941 958	TCGGATGATCCCGGACCAGCCCGGATCTCATCCTGCCCTGCATGGACTGAG R M I P D D Q H S P D L I L P L H G L R	3000
3001 978	GAACGTCAAAGCCATCGACTATGACCCACTGGACAAGTTCATCTACTGGGTGGATGGGCGG	3060
3061 998	CCAGAACATCAAGCGAGCGACGGGACCCAGCCCTTTGTTTTGACCTCTCTGAG Q N I K R A K D D G T Q P F V L T S L S	3120
3121 1018	CCAAGGCCAAAACCCAGACAGCCCCACGACCTCAGCATCTACAGCCGGAC Q G Q N P D R Q P H D L S I D I Y S R T	3180
3181 1038	ACTGTTCTGGACGTGCGAGGCCACCATACCATCAACGTCCACAGGCTGAGCGGGGAAGC L F W T C E A T N T I N V H R L S G E A	3240
3241 1058	CATGGGGGTGGTGCGGGACCGCGACAAGCCCAGGGCCATCGTCGTCAACGCGGA	3300



## FIG. 6G

3301	GCGAGGGTACCTGTACTTCACCAAGATGCAGGACCGGGCAGCCAAGATCGAACGCGCAGC R G Y L Y F T N M Q D R A A K I E R A A	336(
3361 1098	CCTGGACGCCACGAGGTCCTTTCACCACCGGCCTCATCCGCCCTGTGGCCCTT L D G T E R E V L F T T G L I R P V A L	342(
3421 1118	GGTGGTGGACAACTGGGTGTTCTGGGTGGACGCGGACCTGAAGCGCATTGA V V D N T L G K L F W V D A D L K R I E	348( 113 <sup>7</sup>
3481 1138	GAGCTGTGACCTGTCAGGGCCAACCGCCTGACCTGGAGGACGCCAACATCGTGCAGCC	354( 115 <sup>7</sup>
3541 1158	TCTGGGCCTGACCATCCTTGGCATCTTCTTGGATCGACCGCCAGCAGCATGATL	360(
3601	CGAGCGTGTGGAGACCACCGGGGCCAGCGGCCGTGTCGCCCA E R V E K T T G D K R T R I Q G R V A H	366(
3661 1198	CCTCACTGGCATCCAGGGAGGGAGTCAGCCTGGAGGAGTTCTCAGCCCACCCA	372(
3721 1218	TGCCCGTGACAATGGTGGCTGCTCCCACATCTGTATTGCCAAGGGTGATGGGACACCACG A R D N G G C S H I C I A K G D G T P R	378( 1237
3781 1238	GTGCTCATGCCCAGTCCACCTCGTGCTCCTGCAGACCTGTGAGAGAGCCGCC	384(



## FIG. 6H

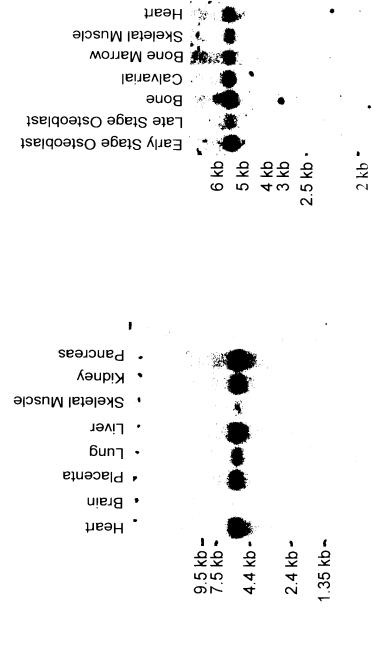
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#### FIG. 61



#### FIG. 6J

4921	TCGGCCGGGCCACTCTGGCTTCTCTGTGCCCCTGTAAATAGTTTTAAATATGAACAAGA	4980
4981	AAAAAATATTTTTATGATTTAAAAATAAAATATAATTGGGATTTTAAAAACATGAGAA	5040
5041	TGTGAACTGTGATGGGGTGGGCAGGGCTGGGAGAACTTTGTACAGTGGAGAAATTTAGTAACTTGGAAAAATTTAGTAAAAAAAA	) L
5101	AAACTTAATTTTGTAAAACA 5120	0



Northern Blot Analysis - Zmax 1

FIG. 7A

Northern Blot Analysis - Zmax 1

FIG. 7B



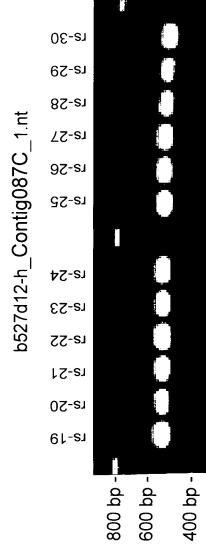


FIG. 8



## ASO Detection of the Zmax1 Exon 3 Mutation

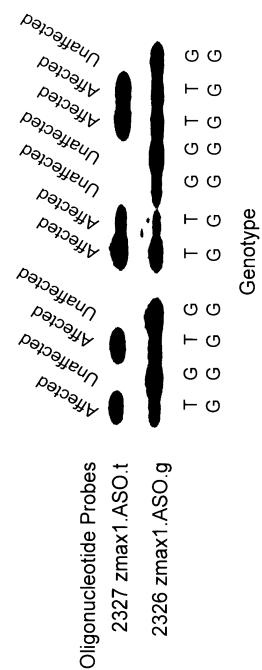


FIG. 9



#### Mouse Zmax1 In situ hybridization 100X Magnification

#### Antisense probe



FIG. 10A

#### Mouse Zmax1 In situ hybridization 100X Magnification

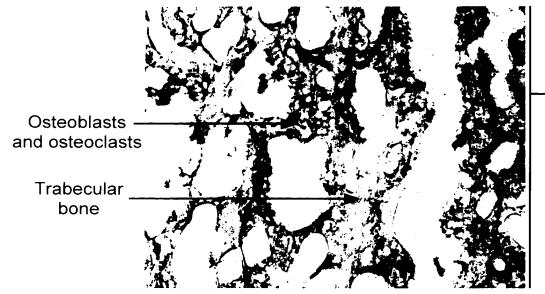
#### Sense probe



FIG. 10B



#### Mouse Zmax1 In situ hybridization 400X Magnification Antisense probe



Proximal Metaphysis

FIG. 11A

#### Mouse Zmax1 In situ hybridization 400X Magnification Sense probe

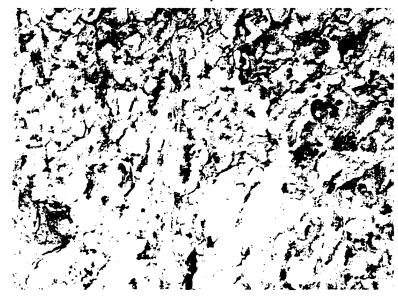
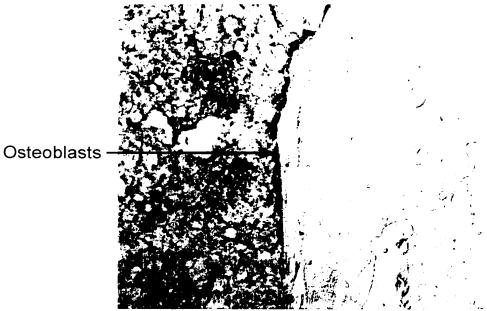


FIG. 11B



#### Mouse Zmax1 In situ hybridization 400X Magnification Antisense probe



Endosteum

FIG. 12A

Mouse Zmax1 In situ hybridization 400X Magnification Sense probe

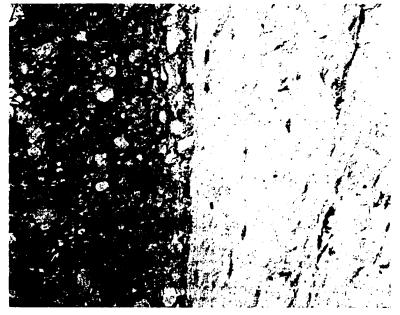
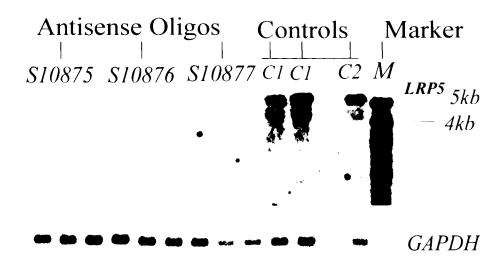


FIG. 12B



#### Antisense Inhibition of Zmax1 Expression



MC-3T3 cells

FIG. 13